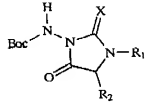
Appl. No. 10/089,329
Atty. Docket No. 7821
Amdt. dated February 5, 2004
Reply to Office Action of January 14, 2004
Customer No. 27752

AMENDMENTS TO THE CLAIMS

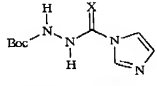
Claims 1 and 2 (cancelled)

3. (Currently Amended) A method for making a hydantoin or thiohydantoin having the formula:

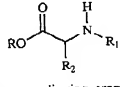


wherein X is oxygen or sulfur, R_1 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; R_2 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; said method comprising the steps of:

a) reacting a hydrazine compound having the formula:



with an amino acid ester having the formula:



R is alkyl, carbocyclic ring, heterocyclic ring, aromatic ring, or heteroaromatic ring, to form a reaction mixture; and

b) heating said reaction mixture to form said hydantoin or thiohydantoin.

4. (Previously Presented) A method according to Claim 3 wherein X is oxygen.

5. (Previously Presented) A method according to Claim 3 wherein said R_1 is a unit selected from the group consisting of phenyl, 4-methoxyphenyl, benzyl, 4-methoxybenzyl, 2-furanylmethyl, 1,3-benzodioxol-5-ylmethyl, (5-methoxy-1*H*-indol-3-yl)ethyl, (1*H*-

imidazol-1-yl)ethyl, (1*H*-imidazol-4-yl)ethyl, [(5-nitro-2-pyridinyl)amino]ethyl, 2-(1-piperidinyl)ethyl, (1-methyl-2-pyrrolidinyl)ethyl, (2-methyl-1-piperidinyl)propyl, 3-(1-piperidinyl)propyl, 3-(4-morphilinyl)propyl, 3-(2-oxo-1-pyrrolidinyl)propyl, (6,6-dimethylbicyclo[3.1.1]hept-3-yl)methyl, 1-(phenylmethyl)-4-piperidnyl, and 2-furanylmethyl.

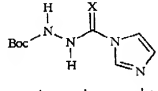
6. (Previously Presented) A method according to Claim 3 wherein said amino acid ester is selected from the group consisting of a benzyl, methyl, or ethyl ester of 2-pipecoline carboxylate, proline, 4-hydroxyproline, 1,2,3,4-tetrahydro-3-isoquinolinecarboxylate, thiozolidine-2-carboxylate, and mixtures thereof.

7. (Previously Presented) A method according to Claim 3 wherein R_2 is hydrogen or methyl.

8. (Previously Presented) A method according to Claim 3 wherein said process is conducted in the presence of a solvent selected from the group consisting of tetrahydrofuran, dimethylformamide, dioxane, methylene chloride, and mixtures thereof.

9. (Previously Presented) A method according to Claim 3 wherein step (b) is conducted at a temperature of from 60 °C to 70 °C.

10. (Previously Presented) A method according to Claim 3 wherein prior to step (a) said process comprises a step of forming said hydrazine compound having the formula:



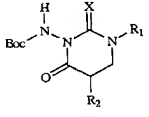
wherein said step comprises reacting tert-butoxycarbonyl hydrazine with carbonyldiimidazole or thiocarbonyldiimidazole to form said hydrazine compound.

11. (Previously Presented) A method according to Claim 10 wherein said hydrazine compound is used in step (a) directly without further purification.

12. (Previously Presented) A method according to Claim 3 further comprising the step of isolating said hydantoin or thiohydantoin.

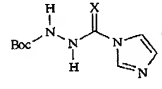
13. (Previously Presented) A method according to Claim 8 wherein said process further comprises the step of removing said solvent.

14. (Currently Amended) A method for making a 3-aminodihydrouracil or 3-aminodihydrothiouracil having the formula:

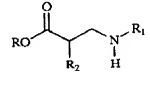


wherein X is oxygen or sulfur, R_1 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; R_2 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; or ~~R_1 and R_2 can be taken together to form a fused heterocyclic ring, a fused aromatic ring, or a fused heteroaromatic ring with the hydantoin or thiohydantoin ring~~ R_1 and the member carbon atom adjacent to the carbon atom containing R_2 can be taken together to form a ring system; said ring system being carboxylic ring, heterocyclic ring, or heteroaromatic ring; said method comprising the steps of:

a) reacting a hydrazine compound having the formula:



with an amino acid ester having the formula:



R is alkyl, carbocyclic ring, heterocyclic ring, aromatic ring, or heteroaromatic ring, to form a reaction mixture; and

b) heating said reaction mixture to form said 3-aminodihydrouracil or 3-aminodihydrothiouracil.

15. (Previously Presented) A method according to Claim 14 wherein X is oxygen.

16. (Previously Presented) A method according to Claim 14 wherein said R_1 is a unit selected from the group consisting of phenyl, 4-methoxyphenyl, benzyl, 4-methoxybenzyl, 2-furanylmethyl, 1,3-benzodioxol-5-ylmethyl, (5-methoxy-1*H*-indol-3-yl)ethyl, (1*H*-imidazol-1-yl)ethyl, (1*H*-imidazol-4-yl)ethyl, [(5-nitro-2-pyridinyl)amino]ethyl, 2-(1-piperidinyl)ethyl, (1-methyl-2-pyrrolidinyl)ethyl, (2-methyl-1-piperidinyl)propyl, 3-(1-piperidinyl)propyl, 3-(4-morphilinyl)propyl, 3-(2-oxo-1-pyrrolidinyl)propyl, (6,6-dimethylbicyclo[3.1.1]hept-3-yl)methyl, 1-(phenylmethyl)-4-piperidnyl, and 2-furanylmethyl.

17. (Previously Presented) A method according to Claim 14 wherein said amino acid ester is selected from the group consisting of a benzyl, methyl, or ethyl ester of 2-pipecoline carboxylate, proline, 4-hydroxyproline, 1,2,3,4-tetrahydro-3-isoquinolinecarboxylate, thiozolidine-2-carboxylate, and mixtures thereof.

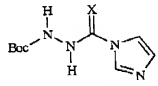
18. (Previously Presented) A method according to Claim 14 wherein R_2 is hydrogen or methyl.

19. (Previously Presented) A method according to Claim 14 wherein said process is conducted in the presence of a solvent selected from the group consisting of tetrahydrofuran, dimethylformamide, dioxane, methylene chloride, and mixtures thereof.

20. (Previously Presented) A method according to Claim 19 wherein said solvent is dioxane.

21. (Previously Presented) A method according to Claim 14 wherein step (b) is conducted at a temperature of from 100 °C to 110 °C.

22. (Previously Presented) A method according to Claim 3 wherein prior to step (a) said process comprises a step of forming said hydrazine compound having the formula:



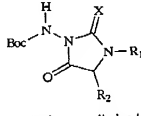
wherein said step comprises reacting tert-butoxycarbonyl hydrazine with carbonyldiimidazole or thiocarbonyldiimidazole to form said hydrazine compound.

23. (Previously Presented) A method according to Claim 22 wherein said hydrazine compound is used in step (a) directly without further purification.

24. (Previously Presented) A method according to Claim 14 further comprising the step of isolating said hydantoin or thiohydantoin.

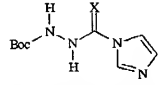
25. (Previously Presented) A method according to Claim 19 wherein said process further comprises the step of removing said solvent.

26. (Previously Presented) A method for making a hydantoin or thiohydantoin having the formula:

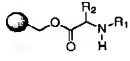


wherein X is oxygen or sulfur, R_1 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; R_2 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; or R_1 and R_2 can be taken together to form a fused heterocyclic ring, a fused aromatic ring, or a fused heteroaromatic ring with the hydantoin or thiohydantoin ring; said method comprising the steps of:

a) reacting a hydrazine compound having the formula:



with a resin-bound amino acid ester having the formula:

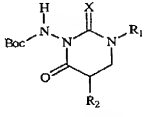


wherein the symbol:

signifies a Merrifield resin, hydroxymethyl, resin, Wang resin, or PEG resin; to form a reaction mixture; and

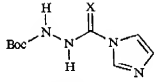
b) heating said reaction mixture to form said hydantoin or thiohydantoin.

27. (Currently Amended) A method for making a 3-aminodihydrouracil or 3-aminodihydrothiouracil having the formula:

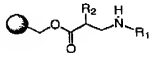


wherein X is oxygen or sulfur, R_1 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; R_2 is hydrogen, alkyl, a heterocyclic ring, an aromatic ring, or a heteroaromatic ring; or ~~R_1 and R_2~~ R_1 and the member carbon atom adjacent to the carbon atom containing R_2 can be taken together to form a fused heterocyclic ring, a fused aromatic ring, or a fused heteroaromatic ring with the 3-aminodihydrouracil or 3-aminodihydrothiouracil ring; said method comprising the steps of:

a) reacting a hydrazine compound having the formula:



with an amino acid ester having the formula:



wherein the symbol:

signifies a Merrifield resin, hydroxymethyl, resin, Wang resin, or PEG resin; to form a reaction mixture; and

b) heating said reaction mixture to form said 3-aminodihydrouracil or 3-aminodihydrothiouracil.